I. General Information

CAS Number: 144-19-4
Name: 1,3-Pentanediol, 2,2,4-trimethyl-
2,2,4-Trimethylpentane-1,3-diol
2,2,4-Trimethylpentan-1,3-diol
2,2,4-Trimetilpentano-1,3-diol
Pentane-1,3-diol, 2,2,4-trimethyl-
2,2,4-Trimethyl-1,3-propanediol
TMPD

II. Physical-Chemical Data

A. Melting Point

Test Substance	
Test substance:	TMPD
Remarks:	
Method	
Method:	Unknown
Remarks:	Data obtained from Hazardous Substances Data Bank Number: 1136
Results	
Melting point value:	51-52 °C
Remarks:	
References	Lide, D.R. (Ed.). CRC Handbook of Chemistry and Physics. 72nd ed. Boca Raton, FL: CRC Press Inc.
Other	Last revision date: 20010809

B. Boiling Point

Test Substance	
Test substance:	TMPD
Remarks:	
Method	
Method:	Unknown
Remarks:	Data obtained from Hazardous Substances Data Bank Number: 1136
Results	
Boiling point value:	234 °C @ 737 MM HG [Peer reviewed]
Remarks:	
References	Lide, D.R. (Ed.). CRC Handbook of Chemistry and Physics. 72nd ed. Boca Raton, FL: CRC Press Inc.
Other	Last revision date: 20010809

C. Vapor Pressure

Test Substance	
Test substance:	TMPD
Remarks:	
Method	
Method:	Estimation
Remarks:	A Modified Grain method
Results	
Vapor pressure value:	0.00291 mm Hg
Temperature:	25 deg C
Remarks:	
References	MPBPWIN v1.40; Meylan, W. (1993). User's Guide for the Estimation Programs Interface (EPI), Version 3.10, Syracuse Research Corporation, Syracuse, New York 13210.
Other	

D. Partition Coefficient

Test Substance	
Test substance:	TMPD
Remarks:	
Method	
Method:	Estimation
Remarks:	
Results	
Log K_{OW}:	1.49
Remarks:	The EPIWIN database also had a referenced value of 1.24
References	KOWWIN v1.66; Meylan, W. (1993). User's Guide for the Estimation Programs Interface (EPI), Version 3.10, Syracuse Research Corporation, Syracuse, New York 13210.
Other	

E. Water Solubility

Test Substance	
Test substance:	
Remarks:	
Method	
Method:	Unknown
Remarks:	
Results	
Value:	19,000 mg/l
Temperature:	25 ^{o}C
Remarks:	Data obtained from Hazardous Substances Data Bank Number: 1136
References	Flick EW; Industrial Solvents Handbook. 4th ed Park Ridge, NJ: Noyes Data Corp p. 452 (1991).
Other	Last revision date: 20010809

III. Environmental Fate Endpoints

A. Photodegradation

Test Substance	
Test substance:	TMPD
Remarks:	
Method	
Method:	Estimation
Test type:	Atmospheric oxidation
Remarks:	
Results	
Temperature:	25 ^{o}C
Hydroxyl radicals reaction	
OH Rate constant:	17.6288 x 10^{-12} cm^3/molecule-sec
Half-life	0.607 Days (12-hr day; 1.5x10^6 OH/cm^3)
Ozone reaction:	No ozone reaction estimation
Remarks:	
Conclusions	Material is oxidized by atmospheric hydroxyl radicals at a rapid rate.
Data Quality	
Remarks:	
References	AopWin v1.90; Meylan, W. (1993). User's Guide for the Estimation Programs Interface (EPI), Version 3.10, Syracuse Research Corporation, Syracuse, New York 13210.
Other	

B. Stability in Water

Reactivity of Trimethyl-1,3-pentanediol (TMPD; CAS# 144-19-4) With Water

This report has been prepared by Dr. Mike Chang of Eastman Chemical to document the known chemistry relevant to the stability of a selected glycol in aqueous solution. The specific glycol addressed in this document is 2,2,4-Trimethyl-1,3-pentanediol (TMPD; CAS# 144-19-4)

Of particular concern in the evaluation of the stability of organic compounds in aqueous solution is the potential for hydrolysis. Hydrolysis is the reaction between water and an organic substrate resulting in the cleavage of existing chemical bonds and subsequent or simultaneous formation of new chemical bonds to form a different chemical compound. Typically, hydrolysis reactions involve incorporation of a water molecule into the structure of the reaction products. For organic substances that participate in hydrolysis reactions, various kinetic methods can be used to monitor the changes in concentration of reactants and determine the rate of transformation of the original substrate into reaction products. OECD Guideline 111 describes one such procedure for measuring the hydrolysis rate of water-soluble substrates as a function of pH. Substrates that exhibit high rates of hydrolysis are considered unstable in an aqueous environment.

TMPD does not participate in hydrolysis reactions. It does not possess labile leaving groups that can be displaced by the nucleophilic attack of a water molecule, as is required in the mechanism of many hydrolysis reactions. Thus, it would not be meaningful to attempt to measure a hydrolysis rate using a protocol such as OECD Guideline 111.

It is conceivable that TMPD will exhibit rearrangement or dehydration under extreme heat and acidic aqueous condition. However TMPD is routinely used to react with acids, such as Isophthalic acids or Adipic acid to form polyester. These reactions were carried out at temperature as high as 215°C and with the formation of water as a by-product. The fact that TMPD can sustain this high temperature in the presence of acids and formation of water lead me to believe any rearrangement or dehydration under moderate temperature and PH is very slow.

Based on the properties of TMPD described above one must conclude that TMPD is not subject to hydrolysis, but may rearrange or dehydrate under extreme conditions. These reactions are expected to be very slow. Therefore, it is my conclusion that TMPD should be considered stable in aqueous solution at temperatures and pH levels relevant to environmental and human exposure.

References:

March, J., ed. "Advanced Organic Chemistry", 3rd edition, p. 831, John Wiley & Sons, New York, 1985.

C. Biodegradation

Test Substance	
Test substance:	TMPD
Remarks:	Purity was 99.0%
Method	
Method:	OECD TG-301A
Test type:	Ready Biodegradability Using the DOC Die-Away Test
GLP:	Yes
Year:	2001
Contact time:	28-Days
Inoculum:	Activated sludge collected from a municipal wastewater treatment plant (Van Lare WWTP, Rochester, NY)
Remarks:	Sodium benzoate at 34.9 mg/L was used as a positive control. TMPD was added to the media at a concentration of 32.6 mg/L for a theoretical concentration of 20 mg DOC/L. DOC concentrations were determined in duplicate for each vessel on days 0,3,7,10,14,17,21,and 28.
Results	
Degradation % at test end:	99% and 100% degradation (replicate A & B) as measured by loss of DOC
Classification:	Readily biodegradable
Remarks:	A lag phase of approx. 3-4 days occurred before biodegradation reached 10% in both test vessels. The test substance reached 91% and 98% degradation within the subsequent 10-day time window. At 28 days the test substance achieved 99% and 100% degradation. The sodium benzoate positive control was degraded 100%. The average incubation temperature was 24 ^{o}C (range 22-26 ^{o}C). Dissolved oxygen (DO) concentration in the media at test start was 9.99 mg/L. At test end the DO concentrations (mg/L) were 8.62 & 8.96 (blanks A&B), 8.76 (positive control), and 8.85 & 9.31 (treatments A&B). Initial pH values were 7.254, 7.529, and 7.526 for the blank, positive control, and test substance, respectively. Test end pH values were 7.33 and 7.30 (blanks A&B), 7.41 (positive control), and 7.32 and 7.34 (treatments A&B). Oscillation speed was an average of 129 ? 0.6 rpm.
Conclusions	Material is considered readily biodegradable under the conditions of this test.
Data Quality	
Remarks:	This was a well-documented OECD guideline study conducted under GLP assurances. One protocol deviation was noted. The temperature of the incubator reached 26 ^{o}C during the study. The deviation did not affect the results of the study.
References	Ready Biodegradability Using the DOC Die-Away Test; Toxicological Sciences Section, Health and Environment Laboratories, at Eastman Kodak Company, Rochester, NY; Study No.EN-112-907039-A, December 7, 2001.
Other	

D. Transport between Environmental Compartments (Fugacity)

Test Substance	
Test substance:	TMPD
Remarks:	
Method	
Test type:	Estimation
Model used:	Level III Fugacity Model; EPIWIN: EQC from Syracuse Research Corporation
Remarks:	
Results	Concentration (%)
Model data and results:	Air 1.99
Estimated distribution	Water 49.4
and media concentration	Soil 48.5
(levels II/III):	Sediment 0.0946
	Physical chemical values and estimated half-life values utilized in this model were default values or obtained from the EPIWIN program.
Remarks:	
Data Quality	
Remarks:	
References	Meylan, W. (1993). User's Guide for the Estimation Programs Interface (EPI), Version 3.10, Syracuse Research Corporation, Syracuse, New York 13210. The Level III model incorporated into EPIWIN is a Syracuse Research Corporation adaptation of the methodology described by Mackay *et al.* 1996; *Environ. Toxicol. Chem.* **15(9)**, 1618-1626 and *Environ. Toxicol. Chem.* **15(9)**, 1627-1637.
Other	

IV. Ecotoxicity

A. Acute Toxicity to Fish

Test Substance	
Test substance:	TMPD
Remarks:	Purity was not available
Method	
Method:	Other
Test type:	Static
GLP:	Yes
Year:	1986
Species/strain:	Bluegill (*Lepomis macrochirus*)
Analytical monitoring:	Yes; temperature, dissolved oxygen, and pH of exposure solutions
Exposure period:	96 hours
Remarks:	Bluegill (n=30) with a mean weight of 0.52 g and mean total length of 36 mm were held for 14 days pre-exposure in well water and fed *ad libitum* until 48-hours prior to exposure. Exposures were conducted for 96-hours in 18.9 L glass aquaria using reconstituted soft water as the dilution water (hardness=41 mg/L, alkalinity = 36 mg/L, pH = 7.2, and conductivity = 165 ?moh/cm). The test solutions were prepared by direct addition of the test material dissolved in acetone to 15 L of dilution water in the aquaria. An aquarium containing the highest amount of acetone used during the dosing was included as a solvent control. The fish were introduced within 20 minutes of dosing at a biomass loading rate of 0.35 g/L. The fish were not fed during the exposure period.
Results	
Nominal concentration:	0, 91, 150, 250, 420, and 700 mg/L
Endpoint value:	96-hour LC_{50} > 700 mg/L
Biological observations:	Observations of the fish were made at 24, 48, 76, and 96 hours. There was 100% survival in the control, solvent control and all exposure concentrations except for the highest exposure concentration (700 mg/L) where 20% mortality was observed at 24 hours. This value did not increase throughout the remaining exposure period.
Statistical methods:	NA, 50% mortality did not occur in any test concentration
Remarks:	The exposure temperature was maintained at 22 ^{o}C, the pH measurements range was 6.7-7.7, and the dissolved oxygen range was 1.4 to 8.6 mg/L. The percent saturation for dissolved oxygen fell below the 40% minimum specified by the test protocol for the control. Since no mortalities or physical stress were observed in the control, it was believed that the deviation did not affect the results of the study.
Conclusions	The LC_{50} value indicates that the test substance would not be classified according to the European Union's labeling directive and would correspond to a "low concern level" according to the U.S. EPA's assessment criteria.
Data Quality	
Reliability:	Reliable without restrictions
Remarks:	Although it is a somewhat older study and lacked some basic information such as test material purity and analytical conformation of test concentrations, it still is a well-documented study conducted under GLP assurances.
References	Acute Toxicity of B0944.01 to Bluegill (*Lepomis macrochirus)*, Springborn Bionomics, Inc., Wareham, MA
Other	

Test Substance	
Test substance:	TMPD
Remarks:	Purity was not available
Method	
Method:	Other
Test type:	Static
GLP:	No
Year:	Unknown
Species/strain:	Catfish (*Corydoras aeneus*), brown trout (*Salmo trutta*), rainbow trout (*Salmo gairdenri*), goldfish (*Carassius auratus*)
Analytical monitoring:	Yes; temperature of exposure solutions
Exposure period:	0.75 – 120 hours
Remarks:	Water was de-chlorinated tap water. Test vessels were cylindrical 20 L glass tanks. Fish were starved for 48 hours prior to test, then exposed to various concentrations and various lengths of time, transferred to clean water and observed for recovery. Catfish: Seven separate experiments, 5 fish/treatment, 1.4 g (avg. wt.), exposure concentrations of 7.5, 7.5, 750, 1000, and 2000 ppm, and exposure periods from 0.75 – 120 hours. Brown trout: Four separate experiments, 5 fish/treatment, 14 or 39 g (avg. wt.), exposure concentrations of 500 and 1000 ppm, and exposure periods of 7 or 8 hours. Rainbow trout: Five separate experiments: 5 or 15 fish/treatment, 1, 15, or 55 g avg. wt., exposure concentrations of 500, 750, or 1000 ppm, and an exposure period of 8 hours. Goldfish: Three separate experiments, 1.5 inch (avg. length), 10 fish/treatment, exposure concentrations of 500, 750, or 1000 ppm, and an exposure period of 8 hours.
Results	
Nominal concentration:	7.5, 75, 500, 750, 1000, 2000 ppm
Endpoint value:	Percent survival
Biological observations:	In all experiments control behavior was normal with no mortalities. Catfish exposed at 7.5 and 75 ppm for 120 hours exhibited no abnormal behavior and 100% survival. Catfish exposed to 750 or 1000 ppm for periods of 7-23 hours all exhibited various symptoms of stress, but recovered very rapidly when transferred to clean water with 100% survival. Catfish exposed to 2000 ppm for 0.75 and 2 hours also exhibited symptoms of stress but recovered within 4 hours with 100% survival. Brown trout: For 14 g fish, survival at 500 and 1000 ppm for 7 hours was 100% and 60% after an 8-hour exposure. For the 39 g wt fish there was 100% survival following and 8 hour exposure to 1000 ppm. Symptoms of stress were observed in all of the brown trout experiments at the 500 and 1000 ppm concentrations. Rainbow trout: Symptoms of stress were observed at all concentrations in all experiments. Three experiments of 8-hour duration were conducted with 1 g fish at concentrations of 500, 750, and 1000 ppm. Survival values were 87%, 100%, and 7% respectively. Two additional 8-hour experiments were conducted at the 1000 ppm concentration with larger trout (15 g or 55 g). Survival in those experiments was 100% (15 g) and 80% (55 g). Goldfish: Three 8-hour exposure experiments were conducted at 500, 750, and 1000 ppm concentrations. Respective survival rates were 100%, 100%, and 20%.

Statistical methods: Remarks:	Unknown Exposure temperature of the catfish experiments was reported as 72 ^{o}F. The temperature ranges for the other species experiments were 46-47^{o}F for brown trout and rainbow trout, and 72-74^{o}F for goldfish.
Conclusions	Exposures of greater than 96 hours with catfish indicated 100% survival at nominal concentrations up to 75 ppm. In exposures of 7 or 8 hours duration, no mortality was observed at nominal concentrations of 750 ppm for catfish, rainbow trout, and goldfish, and 500 ppm for brown trout (750 ppm conc. not tested with this species). At concentrations ? 500 ppm, symptoms of stress were observed, although recovery was relatively rapid when fish were observed after transfer to clean water post exposure in some experiments.
Data Quality Reliability: Remarks:	 Reliable with restrictions Older study lacked some basic information as well as data indicating test material purity and analytical conformation of test concentrations.
References	The Effect of 2,2,4-Trimethylpentanediol on Fresh Water Fish, Laboratory of Industrial Medicine, Eastman Kodak Company, Rochester, NY
Other	

B. Acute Toxicity to Aquatic Invertebrates

Test Substance	
Test substance:	TMPD
Remarks:	Purity was 99.0%
Method	
Method:	OECD 202 and EEC/Annex V C.2
Test type:	Acute immobilization, Static
GLP:	Yes
Year:	2002
Species/strain:	Daphnid/*Daphnia magna*
Analytical monitoring:	Yes; Exposure solutions, temperature, pH, dissolved oxygen
Exposure period:	48-Hour
Remarks:	Water was filter-treated with residual chlorine chemically removed. There were 10 daphnids/dose level. Test was conducted in replicate at each concentration in glass containers. Exposure solutions were submitted for temperature, dissolved oxygen, pH, and concentration verification determinations at 0, and 48 hrs. Observations for signs of immobility and stress were conducted at 0, 24, and 48 hours.
Results	
Nominal concentration:	110 mg/L
Endpoint value:	EC_{50} (48-hr) >109.1 mg/L
Biological observations:	No immobilization was observed during this study
Statistical methods:	NA; No immobilization was observed in either the control or treatment
Remarks:	Exposure temperature ranged from 20-21^{o}C, pH ranged from 8.4 to 8.5, and dissolved oxygen ranged from 8.7 to 9.0 mg/L. The light/dark cycle of the photoperiod was 16 hours on/8 hours off, with a 30-minute transition period.
Conclusions	The EC_{50} value indicates that the test substance would not be classified according to the European Union's labeling directive and would correspond to a "low concern level" according to the U.S. EPA's assessment criteria.
Data Quality	
Reliability:	Reliable without restrictions
Remarks:	This was a well-documented OECD guideline study conducted under GLP assurances.
References	An Acute Aquatic Effects Test with the Daphnid (*Daphnia magna*); Toxicological Sciences Section, Health and Environment Laboratories, at Eastman Kodak Company, Rochester, NY; Study No.EN-431-907039-A, January 22, 2002.
Other	

C. Toxicity to Aquatic Plants

Test Substance	
Test substance:	TMPD
Remarks:	Purity was 99.0%
Method	
Method:	OECD: TG-201 and EEC/Annex V C.3
Test type:	Growth inhibition of algae
GLP:	Yes
Year:	2001
Species/strain:	*Selenastrum capricornutum*
Endpoint basis:	Cell concentrations (biomass) and growth rate
Exposure period:	72-hours
Analytical procedures:	Temperature, light intensity, rpm, and test substance concentration were assessed at the 0, 24, 48, and 72 hours. The pH was assessed at time 0 and after 72 hours.
Results	
Nominal concentration:	110 mg/L
Measured concentration:	110.1 mg/L (geometric mean over all time points)
Endpoint value:	E_bC_{50} and E_rC_{50} (0-72 hr)>110.1 mg/L
NOEC:	The 72 hr NOEC was estimated to be 110.1 mg/L
Was control response satisfactory:	Yes (culture concentrations increased by a factor of 69-fold)
Statistical methods:	The EC_{50} endpoints are calculated by fitting nonlinear regression models to the test data.
Remarks:	A mean illumination of 724 foot-candles was maintained. The mean culture temperature was 24°C and pH ranged from 7.4 to 7.6. Cultures were oscillated at 100 rpm. No protocol deviations were noted.
Conclusions	The 72-hour E_bC_{50} and E_rC_{50} values indicate that, based on this study, the test substance would not be classified according to the European Union's labeling directive and would be classified in a "low concern level" category according to the U.S. EPA's assessment criteria.
Data Quality	
Reliability:	Reliable without restrictions
Remarks:	This was a well-documented OECD guideline study conducted under GLP assurances.
References	A Growth Inhibition Test with the Alga, *Selenastrum capricornutum*; Health and Environment Laboratories, Eastman Kodak Company, Rochester, NY; Laboratory Project ID: EN-512-907039-A; March 1, 2001.
Other	

A. Acute Toxicity

Test Substance	
Test substance:	TMPD
Remarks:	Purity unknown
Method	
Method:	Acute lethality; Other
Test type:	LD_{50} estimate
GLP:	No
Year:	1953
Species/strain:	Rat/Unknown
Sex:	Unknown
Animals/dose:	1
Vehicle:	Corn oil (20% TMPD in vehicle)
Route of exposure:	Oral
Remarks:	Animals were administered a single dose of 400, 800, 1600, 3200, or 6400 mg/kg the test substance by gavage and observed for signs of toxicity over a 14-day period.
Results	
Value:	800-1600 mg/kg
Deaths at each dose:	The animals from the 6400, 3200, and 1600 mg/kg groups died immediately (within 1 hour) after dosing.
Remarks:	Clinical abnormalities included clonic convulsions, gasping, and unconsciousness. However, it is unclear if these abnormalities were observed exclusively in the animals that died or if they were also observed in surviving animals. Both surviving animals gained weight by the end of the study.
Conclusions	Under the conditions of this study, TMPD is slightly toxic when given orally to rats.
Data Quality	
Reliability:	Reliable with restrictions
Remarks:	Purity unknown; sex not specified; insufficient number of animals.
References	Unpublished data, Eastman Kodak Company, Rochester, New York
Other	

Test Substance	
Test substance:	TMPD
Remarks:	Purity unknown
Method	
Method:	Acute lethality; Other
Test type:	LD_{50} estimate
GLP:	No
Year:	1953
Species/strain:	Mouse/Unknown
Sex:	Unknown
Animals/dose:	1
Vehicle:	Corn oil (20% TMPD in vehicle)
Route of exposure:	Oral
Remarks:	Animals were administered a single dose of 200, 400, 800, 1600, or 3200 mg/kg the test substance by gavage and observed for signs of toxicity over a 14-day period.
Results	
Value:	1600-3200 mg/kg
Deaths at each dose:	The animal from the 3200 mg/kg group died within 20 minutes of being dosed.
Remarks:	Clinical abnormalities included weakness, ataxia, gasping, and unconsciousness. However, it is unclear if these abnormalities were observed only in the animal that died or if they were also observed in the surviving animals. All surviving animals either gained or maintained their weight by study termination.
Conclusions	Under the conditions of this study, TMPD is slightly toxic when given orally to mice.
Data Quality	
Reliability:	Reliable with restrictions
Remarks:	Purity unknown; sex not specified; insufficient number of animals.
References	Unpublished data, Eastman Kodak Company, Rochester, New York
Other	

Test Substance	
Test substance:	TMPD
Remarks:	Purity unknown
Method	
Method:	Acute lethality; Other
Test type:	LD_{50} estimate
GLP:	No
Year:	1965
Species/strain:	Rat/Unknown
Sex:	Both
Animals/dose:	4/sex/dose
Vehicle:	Corn oil (20% TMPD in vehicle)
Route of exposure:	Oral
Remarks:	Animals were fasted overnight prior to receiving the test substance at a rate of 3000, 4000, 5000, 6000, or 7000 mg/kg. Animals were administered a single dose by gavage and observed for signs of toxicity over a 14-day period.
Results	
Value:	Not determined (<3000 mg/kg)
Remarks:	Prostration was observed for some of the female rats prior to death on Day 0. All but one male rat from the 3000 mg/kg dose group died by Day 2 of the study. The surviving rat appeared clinically normal for the rema inder of the study.
Conclusions	
Data Quality	
Reliability:	Reliable with restrictions
Remarks:	Purity unknown; inappropriate dose levels.
References	Unpublished data, Eastman Kodak Company, Rochester, New York
Other	

Test Substance	
Test substance:	TMPD
Remarks:	Purity unknown
Method	
Method:	Acute lethality; Other
Test type:	LD_{50} estimate
GLP:	No
Year:	1965
Species/strain:	Mouse/Unknown
Sex:	Male
Animals/dose:	6
Vehicle:	Corn oil (20% TMPD in vehicle)
Route of exposure:	Oral
Remarks:	Animals were fasted overnight prior to receiving the test substance. Animals were administered a single dose by gavage of 1000, 1500, 1800, 2200, 2600, 3100, and 3700 mg/kg and observed for signs of toxicity over a 14-day period.
Results	
Value:	2,200 mg/kg
Deaths at each dose:	All animals from the 3700, 3100, and 2600 mg/kg dose groups died between Days 0 and 3 of the study.
Remarks:	Prostration was observed for two to six animals from all dose groups, except for the 1000 mg/kg group, on the day of dosing. In addition, rapid jerking movements were observed for animals from the 3700 mg/kg group on the day of dosing, prior to death. Animals from the 1000 mg/kg group appeared clinically normal throughout the study, and the surviving animals from all other dose groups appeared clinically normal by Day 3.
Conclusions	Under the conditions of this study, TMPD is slightly toxic when given orally to mice.
Data Quality	
Reliability:	Reliable with restrictions
Remarks:	Purity unknown; only one sex tested.
References	Unpublished data, Eastman Kodak Company, Rochester, New York
Other	

Test Substance	
Test substance:	TMPD
Remarks:	Purity unknown
Method	
Method:	Acute lethality; Other
Test type:	LD_{50} estimate
GLP:	No
Year:	1965
Species/strain:	Guinea pig/Unknown
Sex:	Male
Animals/dose:	6
Vehicle:	Corn oil (20% TMPD in vehicle)
Route of exposure:	Oral
Remarks:	Animals were fasted overnight prior to receiving the test substance. Animals were administered a single dose by gavage of 1000, 1500, 1800, 2200, 2600, and 3100 mg/kg and observed for signs of toxicity over a 14-day period.
Results	
Value:	1,800 mg/kg
Deaths at each dose:	All of the animals from the 3100 and 2600 mg/kg groups and approximately half of the animals from the 2200 and 1800 mg/kg groups died between Days 0 and 1 of the study.
Remarks:	Clinical abnormalities included prostration, weakness, labored respiration, tremors, and rough haircoat. These abnormalities did not persist beyond Day 1 of the study, either because the animals died or recovered. All animals from the 1500 and 1000 mg/kg groups and 1 or 2 animals from the 2200 and 1800 mg/kg groups, respectively, survived to study termination.
Conclusions	Under the conditions of this study, TMPD is slightly toxic when given orally to guinea pigs.
Data Quality	
Reliability:	Reliable with restrictions
Remarks:	Purity unknown; only one sex tested.
References	Unpublished data, Eastman Kodak Company, Rochester, New York
Other	

Test Substance	
Test substance:	TMPD
Remarks:	Purity unknown
Method	
Method:	Acute lethality; Other
Test type:	LC_{50} estimate
GLP:	Yes
Year:	1965
Species/strain:	Rat/Unknown
Sex:	Unknown
Animals/sex/dose:	4
Route of exposure:	Inhalation
Remarks:	Rats were exposed to 4.5 mg/L TMPD for a single 6 hour time period. A Wright Dust Feed Mechanism was used to generate particles that were directed into an 18.5 L exposure chamber at 5 L/min. Chamber temperature was 25 ?C. Particle size determination revealed that 34.1% of particles were respirable. Total dose respired was estimated to be 2.8 g/kg. (The report did not include documentation as to how the "total dose respired" value was obtained.)
Results	
Value:	LC_{50} >4.5 mg/L
Deaths at each dose:	No mortality was observed.
Remarks:	Clinical abnormalities observed during exposure included piloerection, vasodilation, lacrimation, and nose rubbing. All animals gained weight by study termination.
Conclusions	Under the conditions of this study, TMPD only produces minimal ocular and nasal irritation following inhalation exposure.
Data Quality	
Reliability:	Reliable with restrictions
Remarks:	Sex not specified; insufficient number of animals; insufficient dosage information; no information on particle size.
References	Unpublished data, Eastman Kodak Company, Rochester, New York
Other	

B. Repeated Dose Toxicity

Test Substance	
Test substance:	TMPD
Remarks:	Purity was unknown.
Method	
Method:	Other
Test type:	Repeated exposure
GLP:	No (Pre-GLP)
Year:	1967
Species/strain:	Rat/CFE
Route of exposure:	Oral
Duration of test:	60-Days
Dose levels:	0, 0.5, 1.0, 2.0%
Sex:	Both (15/sex/dose level; 60/control)
Frequency of treatment:	Daily in diet
Control group and treatment:	Yes; 5% Mazola corn oil
Post-exposure observation period:	None
Remarks:	Rats were fed TMPD diets for 30 days. At the end of 30 days, all animals from the 1.0% dose group and 15 animals per sex from the control group were used for a fertility study. The remaining animals were treated for an additional 27 days prior to be euthanized on Day 60. Body weights and feed consumption were measured at approximately one-week intervals. On Day 55, blood was collected from 10 animals per sex from the 2.0% and control groups for hematology and clinical chemistry analysis. Selected organs were collected weighed and examined for histopathology.
Results	
NOAEL:	0.5%
Toxic responses by dose:	One female rat from the 2.0% dose group and two male rats from the control group died during the study. The death of the female rat was attributed to a laboratory accident, and not considered treatment-related. The behavior, appearance, appetite and stools of all other animals remained normal throughout the study. Mean body weight gains were significantly decreased in females and slightly decreased in males exposed to the 2.0% diet. This was accompanied with decreases in food consumption. Mean absolute and relative liver, kidney, and adrenal gland weights were significantly higher for male rats from the 2.0% dose group, and mean absolute lung weights were significantly lower for male rats from the 2.0 and 0.5% dose groups (there was no effect on lung to BW ratios). Mean absolute and relative liver and adrenal gland weights and relative kidney, heart, and brain weights were significantly higher for female rats from the 2.0% dose group when compared with the control group. The mean relative lung weight was significantly lower for female rats from the 0.5% dose groups (absolute values were normal). No biologically significant differences were noted for hematology or clinical chemistry values for any of the treated groups, and no gross or microscopic lesions attributed to treatment with the test substance were observed.
Statistical methods:	Analysis of variance and Duncan's New Multiple Range Test.
Remarks:	The 0.5% dose was chosen as a NOAEL as the only effect noted at this level was a decrease in lung weight. This change was present in males only when analyzed on an absolute weight basis but not on a relative to BW basis. In females no effect on absolute lung weight was seen at any dose whereas a change in relative weight occurred only at the 0.5% level. The histological appearance of the lungs was normal at all exposure levels.

Conclusions	Limited signs of toxicity were observed in male and female rats administered TMPD in the diet for 57 days.
Data Quality	
Reliability:	Reliable with restrictions
Remarks:	No analytical data on test mixtures that indicate stability, homogeneity, or purity, limited detail of study results.
References	Unpublished data, Eastman Kodak Company, Rochester, New York
Other	

C. Genetic Toxicity – Mutation

Test Substance	
Test substance:	TMPD
Remarks:	Purity was >98.95%
Method	
Method:	OECD:TG-471
Test type:	*In vitro* mutagenicity
GLP:	Yes
Year:	2001
Species/strain:	*Salmonella typhimurium*/TA98, 100, 1535, 1537, and *Escherichia coli*/WP2*uvr*A
Metabolic activation:	Yes; Aroclor 1254-induced SD rat liver S9
Concentration tested:	Maximum concentration tested was 5000 ug/plate
Remarks:	Positive controls (benzo[a]pyrene, 2-aminoanthracene, 2-nitrofluorene, sodium azide, 2-aminoanthracene, ICR-191, and 4-nitroquinoline-N-oxide) were run concurrently. DMSO was used as a vehicle control.
Results	
Result:	No positive responses were induced in any of the tester strains
Cytotoxic concentration:	>5000 ug/plate (no evidence of cytotoxicity was seen)
Precipitation concentration:	No precipitate was noted at the highest concentration tested.
Genotoxic effects	
With activation:	Negative
Without activation:	Negative
Statistical Methods:	Mean number of revertants and standard deviations were calculated. Various criteria were established to constitute a valid assay and a positive response was indicated by a 2-3 fold increase in mean revertant number dependent on the bacterial tester strain.
Remarks:	All criteria for a valid study were met.
Conclusions	Material was not genotoxic under conditions of this assay.
Data Quality	
Reliability:	Reliable without restrictions
Remarks:	This was a well-documented OECD guideline study conducted under GLP assurances.
References	Covance Laboratories Inc., Vienna, VA; Study No.: 21781-0-409OECD; May 15, 2001
Other	

D. Genetic Toxicity – Chromosomal Aberrations

Test Substance	
Test substance:	TMPD
Remarks:	Purity was >98.95%
Method	
Method:	OECD: TG-473
Test type:	*In vitro* mammalian chromosomal aberrations assay
GLP:	Yes
Year:	2000
Species/strain:	Chinese hamster ovary cells (CHO)
Concentrations tested:	10.2 to 1500 ug/ml (this level exceeds the 10 mM max. recommended level)
Metabolic Activation:	Yes; Aroclor 1254-induced SD rat liver S9
Remarks:	The positive controls consisted of mitomycin-C and cyclophosphamide. Negative control was the test vehicle water.
Results	
Result:	No significant increases in cells with chromosomal aberrations, polyploidy, or endoreduplication were observed in the analyzed cultures at any concentration.
Cytotoxic concentration:	>1500 ug/ml (no signs of toxicity were noted)
Precipitation concentration:	No precipitate was observed at the maximum concentration tested.
Genotoxic effects	
With activation:	Negative
Without activation:	Negative
Statistical methods:	Statistical analysis employed a Cochran-Armitage test for linear trends and Fisher's Exact Test to compare the percentage of cells with aberrations.
Remarks:	
Conclusions	Material was not genotoxic (did not induce any structural or numerical aberrations) under conditions of this assay.
Data Quality	
Reliability:	Reliable without restrictions
Remarks:	This was a well-documented OECD guideline study conducted under GLP assurances.
References	Covance Laboratories Inc., Vienna, VA; Study number: 21781-0-437OECD; November 20, 2000.
Other	

E. Developmental Toxicity

Test Substance	
Test Substance:	TMPD
Remarks:	Purity unknown
Method	
Method:	Other
Type of Study:	3-Generation Developmental/Reproductive Toxicity Study
GLP:	No
Year:	1974
Species/Strain:	Rat/unknown
Sex:	Both
Route of Exposure:	Oral, diet
Dose Levels:	1.0%
Duration of Test:	3-Generations
Frequency of Treatment:	Daily
Control Group:	5% Mazola corn oil
Remarks:	Groups of 15 rats/sex were fed diets containing either 0.0 or 1.0% test substance for 30 days as part of a sub-chronic repeated dose toxicity study, before being transferred to the reproductive phase of the study. These animals were designated as the parent generation (F_0), and were mated twice for two groups of first generation litters (F_{1a} and F_{1b}). Fifteen animals per sex, per group were selected from the F_{1a} litters and mated twice to produce two groups of second-generation litters (F_{2a} and F_{2b}). This process was repeated with the F_{2a} animals to produce two groups of third generation litters (F_{3a} and F_{3b}). However, due to a questionable mortality rate seen in the F_{3a} litters at one week postpartum, the F_{2a} dams were allowed to litter and mate a third time to produce a third group of third generation litters (F_{3c}). The F_{3c} pups were collected by laparotomy on the Day 19 of gestation. All animals were maintained on their assigned diets throughout the entire study. The data recorded for each generation included: the number of inseminations and pregnancies, mean gestation period, and litter size and mortality at birth, weaning, and one and two weeks after weaning. Mean pup body weights were measured at weaning, one and two weeks post-weaning, and at the time of necropsy. The pups in all litters from each generation, except for those that had been selected to be breeders, were euthanized and necropsied at 7 weeks of age. All breeders were euthanized and necropsied shortly after they had produced the required groups of litters. All animals were examined for gross pathology, and selected tissues were collected from two male and two female rats from each litter. Resorption sites were counted for the F_{2a} dams, and the numbers of viable and dead fetuses were recorded for the F_{3c} litters. The F_{3c} fetuses were examined for gross abnormalities, weighed, and placed in either a 95% ethanol fixative or Bouin's fixative.
Results:	
Maternal toxicity NOAEL:	1.0%. Percentages of inseminations, pregnancies, average gestation period, and litter size were comparable among treated and control groups.
Repro./Develop. toxicity NOAEL:	1.0%.

Postnatal toxic responses:	Pup mortality rates from birth to two weeks post-weaning were erratic across generations. Treated litters from three generations (F_{1b}, F_{2a}, F_{3a}) had significantly higher mortality rates than the control group; treated litters from two generations (F_{1a}, F_{3b}) had mortality rates that were comparable to the control group; and treated litters from one generation (F_{2b}) had a significantly lower mortality rate than the control group. In the majority of these cases, the mortality was the result of the loss of one or two litters. Mean pup body weights were significantly lower for litters from the F_{1a} generation at two weeks post-weaning, and for litters from the F_{2b} generation from weaning to necropsy (7-9 weeks of age). No gross lesions or developmental effects were observed at necropsy.
Statistical Methods:	Statistical detail was not mentioned although some data were noted as being significant based on Students "t" test and "two x two X^2.
Remarks	
Conclusions	Animals given test diets containing 1.0% TMPD throughout three generations did not result in developmental or reproductive toxicity.
Data Quality	
Reliability:	Reliable with restrictions.
Remarks:	Study lacked a significant amount of methodology documentation and detail.
References	Unpublished data, Eastman Kodak Company, Rochester, New York
Other	

F. Toxicity to Reproduction

See robust summary E above which was a combined developmental/reproductive toxicity screening assessment.